Cosmetical and therapeutic compositions

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Resumen

Therapeutic and cosmetic preparations, dentifrices, depilatories, hair lotions and tonics etc. comprise cytochrome or a cytochrome-active water-soluble derivative of cytochrome, which includes the dicysteine-porphyrin ring of cytochrome c, distributed in a pharmaceutically acceptable carrier. Cytochromes specifically mentioned are cytochrome a, cytochrome a1, cytochrome a2, cytochrome a3, cytochrome b, cytochrome b2 and cytochrome c. There may optionally be present in the therapeutic preparations (a) sulphonamides, e.g. sulphanilamide, sulphathiazole, sulphaguanidine, carboxy-sulphathiazole, sulphadiazine, sulphamerazine and sulphapyridine, (b) benzoic acid compounds, e.g. n - propyl p - hydroxybenzoate, methyl p - hydroxybenzoate, p-aminobenzoic acid, methyl p-aminobenzoate, n-propyl p-aminobenzoate and n-amyl p-aminobenzoate, (c) antibiotics, e.g. penicillins and esters thereof, streptothrycin, bacitracin, streptomycin, vivicillin, gramicidin, actinomycin, tyrothricin, subtilin, tyrocidine, kojic acid, terramycin and their salts, (d) hormones, e.g. cortisone, hydrocortisone acetate, gonadotropic hormones, androgenic hormones and stilboestrol, (e) enzymes, e.g. pepsin, trypsin and lysozyme, (f) other substances such as cysteine, glutathione, urea, allantoin, alloxan and Vitamin E. The therapeutic preparations may be applied topically or orally, and may also be used in the form of suppositories or chewing gum. The cosmetic forms include face creams, hand lotions, lipsticks, rouge and finger nail conditioners. A process for the preparation of cytochrome c from ox heart is described.

Descripción

COMPLETE SPECIFICATION
Cosmetical and Therapeutic Compositions
I, DAVID AGNEW VOGEL, of 2000 Palmgren Drive, Glenview, Illinois, United States of America, a citizen of the United States of America, do hereby declare the invention, for which I pray that a patent may be granted to me, and the method by which it is to be performed, to be particularly described in and by the following statement: -
This invention provides cosmetical and therapeutical preparations.

In this specification, except where the context requires that it should bear another meaning, the word "cytochrome" means "cytochrome or a cytochrome-acuve watersoluble derivative of cytochrome which includes the dicysteine-porphyrin ring of cytochrome c".

The present invention provides a cosmetical or therapeutic composition with comprises cytochrome as hereinbefore defined, distributed in a pharmaceutically acceptable carrier. Preferably, the cytochrome is cytochrome c.

In a preferred embodiment, the cytochrome as hereinbefore defined is distributed in a pharmaceutically acceptable ointment carnet
A further provision of the invention is a dentifrice comprising a pharmaceutically acceptable powder base or plastic body mass having cytachrome (as hereinbefore defined), distributed throughout said base or mass.

Also within the purview of this invention is a dusting powder having cytachrome (as hereinbefore defined) distributed throughout the mass thereof.

The present invention also provides a therapeutic composition useful in treating ulcerous wounds, which comprises cytachrome as hereinbefore defined together with a promoter which enhances the therapeutic activity thereof, said cytachrome and promoter being distributed in a pharmaceutically acceptable viscous ointment carrier.

The compositions of this invention are particularly useful in the field of cosmetology. It has been found that cytochrome as hereinbefore defined possesses cosmetological properties which makes it especially suitable for use in face creams, hand lotions, dentrifices and dusting powders.

The cosmetical compositions of this invention are excellent skin and finger nail conditioners. These novel compositions promote good complexion of the skin and more uniform, stronger finger nails.

Various solutions, e.g. aqueous and alcolsolic aqueous solutions, of cytachrome (as hereinbefore defined) can be used as face lotions for use after shaving or for use as a cleansing medium. Alternatively, the cytochrome can be incorporated in shaving soap or cream. Other examples of the use of cytachrome as hereinbefore defined on the face include cold creams and cleansing creams, as well as lotions, lipsticks, rouge and various cream masks.

Hand creams including cytochrome as hereinbefore defined in cosmetologically active amounts have been successful in the treatment of chapped hands.

In the form of ointments, this invention is useful in treating various scalp disorders and infections and as a hair ointment or tonic. Alternatively, the cytochrome as hereinbefore defined may be incorporated in a hair shampoo or hair dyes and hair bleaches for application in that manner. It further is contemplated that various aqueous solutions containing cytochrome as hereinbefore defined and alcoholic aqueous solutions containing cytochrome as hereinbefore defined can be used as a hair tonic and scalp lotion.

Aqueous solutions and particularly iso-tonic saline solutions containing cytochrome as hereinbefore defined can be used for treatment of the eye. For example, an eye wash or eye lotion would comprise cytochrome as hereinbefore defined dissolved in a suitable aqueous solution.

Preferably, the compositions of the present invention contain a bactericide.

The compositions of this invention are also useful as oral cleansing preparations and impede and

cause cessation of the action of decay in the oral dental recesses and of bacterial action in the oral cavity generally. These nesv compositions also promote the formation of normal, heafthy tissue throughout the oral cavity and the elimination of unpleasant odours therein.

An aqueous solution containing cytochrome as hereinbefore defined is useful as a mouth wash. Aqueous solutions containing cytochrome as hereinbefore defined are also useful as sprays for the oral cavity and particularly as deodorizing sprays.

Various preparations containing cytochrome as hereinbefore defined are also effective in treating various external openings, such as nasal passages and ear passages.

For example, an aqueous solution containing cytochrome as hereinbefore defined could be used as a nasal spray or as nose drops.

It further is contemplated that cytochrome as hereinbefore defined be used as the active ingredient in a spray fror use under the arm pits and in depilatories.

Cytochrome as hereinbefore defined can also be effectively applied to certain of the areas of the mouth and by incorporating the cytochrome in a suitable confection.

For example, cytochrome can be effectively incorporated in lozenges, cough drops and chewing gum for treatment of the oral cavity and the throat passages.

Certain of the compositions of this invention are adapted for topical application and they are effective in the treatment of lesions. These compositions have bactericidal properties and promote the growth of tissue cells, particularly healthy, granulation tissue in lesions.

The term "cytochrome", unless qualified includes all of the known forms of this class of pigments and includes specifically cytochrome a, cytochrome cue,, cytochrome 2, cytochrome a,, cytochrome b, cytochrome b,, and cytochrome c. The chemistry of these compounds is very complex and has not been completely investigated. Cytochrome c has been most thoroughly investigated and is found according to the most recent authorities to consist of four pyrrole nuclei and four carbon atoms forming a closed ring, the pyrrole nuclei and carbon atoms alternating around the ring and having various substituent groups attached thereto. It is believed that all of the cytochromes are structurally similar or can actually be derived from or theoretically could be
derived or prepared from cytochrome c. The structure of cytochrome c is believed to be as follows:

This molecule can be characterized as a dicysteineporphyrin having long protein chains R1 and R2 attached to each of the crysteine radicals, respectively. Each of the protein chains has been calculated to contain 96 T 1 amino acid residues, of which 21 or 22 are lysine residues. There are nine or 10 free e -amino groups and probably the molecules contain this many polypeptide chains. The other amino acids and the number thereof present in each protein chain are as follows: histidine, 3; arginine, 2; cysteine, 1; tyresine, 5; tryptophan, 2; glutaric and aspartic acid, 19; leucine fraction 9; alanine + glycine + valine + hydroxyvaline fraction 33. The iron porphyrin has been illustrated and is the natural occurring product. However, suitable reactions can be utilized to change this nuclear metal to some other metal such as magnesium, iron, and silver.

Cytochrome in the reduced condition shows a characteristic absorption spectrum with four bands, the positions of which are approximately the same regardless of the source of the cytochrome. These bands appear at the following points: 6019 A., 5665
A., 5502 A., and 5210A. It is believed that none of the individual pigments can produce all four of these bands but instead a mixture of the pigments results in this characteristic absorption spectrum of cytochrome.

The cytochromes are widely dispersed in both the animal and vegetable living organisms. Cytochrome has been found in striated muscles of animals and birds, in baker's yeast, in molluscs, crustacea, 40 species of insects, various tissues of higher animals, bacteria, various bulbs of plants, potatoes, grains of wheat, barley, oats and stamens of young flowers. The better sources of cytochrome are pigeon breasts, beef heart, pig shoulder, beef tongue, beef shoulder and yeast. In general, the more active the tissue the greater the cytochrome concentration.

A preferred method of preparing cytochrome c for use in the present invention is as follows: Ox heart is freed from fat and ligaments and is then very finely minced.

1,100 grams of the ox heart is mixed with 1,100 cc. of 0.15 N trichloroacetic acid and permitted to stand for two hours at room temperature with occasional stirring.

The pH during this step is approximately pH4. After standing for two hours, the liquid is removed by pressure, treated with sodium hydroxide until the reaction mass has a ply7, and then centrifuged. The resulting clear liquid contains reduced cytochrome and a small amount of oxyhaemoglobin. Ammonium sulphate is added thereto to precipitate the oxyhemoglohin, 50 grams of ammonium sulphate being added to each 100 cc. of solution. The solution is filtered, again treated with ammonium sulphate (5 grams being added for each 100 cc. of solution), and left over-night in an ice chest.

The pH at this point is approximately 4.9. The liquid is then filtered and, while still cold, mixed with 1/40 its volume of 20 percent trichloroacetic acid to bring the pH to 3.7. Within ten minutes oxidized cytochrome precipitates completely and is collected as a bright red deposit by centriftigation for 10 minutes. The precipitated product is shaken with 500 cc. of saturated ammonium sulphate solution and again collected by centrifugation. The cytochrome is then transferred to a "Cellophane" (registered Trade Mark) sack with approximately 20 cc. of distilled water and dialyzed for two days at 40C. against a 1 percent sodium chloride solution. After the end of two days, the contents of the sack are shaken with a few drops of chloroform and filtered.

Approximately 30 cc. of a clear, dark-red solution is obtained, containing 0.182 grams of cytochrome c with an iron content of 0.34 percent. The cytochrome c prepared by this process has an equivalent weight of 16,500 and by osmotic pressure determination approximately a molecular weight of also 16,500.

A somewhat purer product can be obtained by the modified procedure of Keilin and Hartree described in Proceedings Royal Society (London) B, 122, 298 (1937).

It is to be understood that the various cytochromes described herein as suitable for use in accordance with the present invention may be used alone or in mixtures. In fact, the material usually employed is a mixture of two or more cytochrome compounds.

This is true because it is difficult to isolate a specific cytochrome and isolation only serves to increase the cost from the standpoint of the present invention without increasing the utility. The preferred cytochrome and the cytochrome which is at least the major component of the product obtained by the modified method described above is cytochrome c.

The cytochrome obtained from this modified process is water-soluble.

It is preferable to employ relatively highly purified forms of cytochrome in the compositions of the present invention. Attention is particularly directed to this fact in view of the normal occurrence of cytochrome in combination with complex cell materials which tends to result in relatively impure extracts. By relatively highly purified forms of cytochrome is meant cytochrome having a purity of 10 percent or greater. It is preferable that the cytochrome has eliminated or separated therefrom as much as possible of cellular material and other inactive substances which may tend to interfere with the properties of the cytochrome. It is to be noted that the cytochrome derived by the methods above described has very high purity (of the order of 90 percent or more).

The water soluble derivatives of cytochtome are preferably incorporated in a composition wherein the base is hydrophilic. The "Carbowax" (registered Trade Mark) ointment base and the lanolin base described hereinafter are examples of such hydro philic bases. If it is desired to use water-insoluble derivatives, it is preferred to use nonhydrophilic bases such as the solid hydrocarbon bases.

The present invention is particularly directed to bases that are viscous or nonflowing at ordinary room temperatures. The purpose of using such a base is to permit topical application for prolonged periods of time. Lanolin (wool fat), in a purified either hydrous or anhydrous condition is a preferred medicament base. Instead of the lanolin, however, many equivalent fats and unguents may be employed including for example. lard or Aquaphor (mainly eucerin, which comprises a mixture of esters of iso- or oxy- cholesterol alcohols with principally oleic, carnaubic and myristic acids).

The unctuous preparations may also comprise petrolatum, monolene and the like, as well as cholesterols, stearates, palmitates and other higher and lower fatty acids and alcohols and their esters, such as triacetin and particularly the more or less viscous alkyl alcohols corresponding to both the high and lower fatty acids and the glycerol esters of the higher fatty acids, such as glycerol stearate, glycerol palmitate and glycerol oleate. It is preferable to employ substances that are bland, non-irritating and substantially isotonic with the body fluid of the region to which they are applied. The

foregoing materials are moreover normally neutral in the presence of water.

Amounts of cytochrome as small as 0.001 grams per 100 grams of base have been found sufficient to give a preparation having cosmetical or therapeutic properties.

On the other hand, relatively high concentrations of cytochrome of the order of 50 percent by weight based on the total weight of the composition have been found effective and have been found to result in no harmful irritation of the tissues. Thus virtually any desired amount of cytochrome may be present provided it is sufficient to give the composition cosmetical or therapeutic properties. A preferred range of cytochrome concentration is from 0.01 percent to 10 percent by weight of the composition. The most economical range of cytochrome concentration is from 0.01 percent to 3 percent by weight of the final composition.

The following Examples illustrate the compositions of this invention.

EXAMPLE I
"Carbowax 4,000" 30 grams
"Carbowax 1,500" 32 grams
Propylene Glycol 30 grams
Water 7 ml.

Cytochrome 1 gm.

The "Carbowaxes" are non-volatile polyethylene glycols soluble on both water and aromatic hydrocarbons.

The cytochrome used in this preparation is the product obtained by using the modified extraction procedure of Keilin and Hartree set forth above.

The "Carbowax 4,000" and the "Carbowax 1,500" are melted together by applying heat. The cytochrome is soluble in water and is dissolved in the water which forms part of the composition. The aqueous solution of cytochrome is then mixed with the propylene glycol and the resultant mixture added to the melted "Carhowaxes". After suitable stirring to obtain uniform distribution of the cytochrome throughout the base, the product is poured into containers and allowed to cool. Upon cooling, the preparation solidifies to form a viscous mass which is non-flowing at room temperature.

Preferably, a fresh sample of cytochrome is utilized in making the preparation. It is also desirable to avoid subjecting the cytochrome to high temperatures in preparing the medicament base. Accordingly, the melted mixture of "Carbowaxes" is cooled to as low a temperature as possible while still maintaining fluidity. It has been found that this mixture of "Carbowaxes" can be successfully cooled to about 350C. before adding the mixture containing the cytochrome and still obtain good distribution of the cytochrome throughout the medicament base. Heating the cytochrome to high temperatures tends to impair its wound healing properties.

ExAMPLE II
1 gram of cytochrome employed in the preparation of Example I was thoroughly mixed into 100 grams of lanolin which contained about 5 percent of water. The lanolin had previously been heated over a water bath at 350 C. until it melted and was maintained at this temperature during the addition of the cytochrome.

EXAMPLE III
900 grams of anhydrous lanolin and the 225 grams of U.S.P. white petrolatum were melted together in a double boiler. In a separate container a solution was made by mixing 10 grams of the cytochrome employed in the preparation of Example I with 50 ml. of water. The cytochrome solution was added to the melted material in the double boiler with vigorous stirring. The preparation was then poured into jars and cooled to room temperature.

EXAMPLE IV The composition was prepared in accordance with the procedure and using the same ingredients as Example I except that 0.1 gram of cytochrome was used.

EXAMPLE V
The composition was prepared in accordance with the procedure and using the same ingredients as Example I except that the following parts by weight were untilized:
"Carbowax 4000" 30 parts
"Carbowax 1500" 40 parts

Propylene glycol 20 parts
Water 10 parts
Cytochrome 0.2 parts
EXAMPLE VI
"Dermabase" 100 parts by weight
Water 2 parts by weight
Cytochrome 0.1 part by weight
"Dermabase" is a specialized emulsion of fatty acid esters and alcohols. In preparing the composition, the cytochrome is first dissolved in the water. The "Dermabase" is then melted and thereafter the aqueous solution of cytochrome is added thereto. After suitable mixing and stirring the composition while molten was poured into tubes and jars where it was cooled.

The following are specific Examples of the present invention in dentrifices.

EXAMPLE VII 5 grams of "Castile" (registered Trade Mark) soap powder and 0.5 grams of gum tragacanth were carefully ground together into 20 cc. of distilled water. 1 gram of finely divided cytochrome was then carefully mixed in. Finally, 20 cc. of glycerine, 53 grams of precipitated chalk and 1.5 grams of flavoring oils, including oil of wintergreen and saccharine to taste, were added and evenly distributed in the mixture to provide a uniform composition. This composition is a paste dentifrice adapted to be applied in the usual manner of using paste dentifrices.

EXAMPLE VIII
Another paste dentifrice was made exactly as described in Example VII except that in place of the 0.5 grams of gum tragacanth, 0.5 grams of pectin was used. This paste dentifrice has been found to have the particular advantage of remaining for relatively long periods on surfaces in the oral cavity with which it comes in contact.

This invention includes within its scope other paste oral cleansing preparations than those described in the above examples and, in general, the cytochrome may be included in any desired oral cleansing preparation containing liquid whereby it is of pasty consistency. More particularly, it has been found that without detriment to the novel action of the cytochrome, the oral cleansing preparations containing cytochrome may include, in addition to the cytochrome and liquid, one or more other ingredients such as detergents, abrasives, thickeners, soaps, flavoring materials, antienzyme action agents, fluorides and other conventional ingredients of oral cleansing preparations. The additional ingredients mixed with the cytochrome and paste preferably will include materials which act particularly to distribute the cytochrome in localized contact with recesses, cavities or pockets wherein decay normally occurs.

Among the other conventional ingredients which may be added are such thickeners or gummy materials as gum tragacanth and gum arabic. The detergent employed instead of being a neutral soap powder such as "Castile", may be a detergent formed from a sulfonated higher fatty acid. Where a mild dental abrasive action is desired, the use of precipitated chalk is indicated. It has been found that the addition of hygroscopic material, such as glycerine, facilitates contact of the cytochrome with remote tissue surfaces and tends to maintain this contact even in the presence of a substantial discharge.

The relative proportions of the various ingredients in a tooth paste may vary considerably from those given in Examples VII and VIII without adverse results so long as a substantial amount of cytochrome is present. Thus, amounts of cytochrome as small as 0.01 percent by weight have been found sufficient to give the oral cleansing preparations cosmetical properties. It is preferable, however, to include a quantity of cytochrome on the order of 0.1 percent based on the total weight of the oral cleansing preparation. While greater or lesser amounts than the foregoing may be used, it is apparent that if the quantity is too small the improvement in cosmetical properties will not be substantial. On the other hand, the use of large amounts, while not usually harmful, does not greatly increase the cosmetical effect as compared with quantities on the order of about 0.1 percent to about 3.0 percent based on the weight of the oral cleansing preparation.

The cytochrome compositions of the present invention are adapted for use generally in cell stimulating compositions that are viscous and nonflowing at room temperatures whereby they are useful in topical application for promoting the growth of normal healthy cells. They are particularly adapted for use in the treatment of ulcerous wounds and to this end are applied locally to the affected area. It is preferable to employ the cytochrome compositions so as to cause the wound to heal from the base, particularly where the wound is deep.

Various promoters may be incorporated with the cytochrome compositions described above to produce a therapeutic agent exhibiting increased therapeutic activity.

The promoters to be incorporated in cytochrome compositions in accordance with the present invention include the following groups of materials:
A. Chemical agents such as the sulfonamides, other organic sulphur compounds, benzoates such as hydroxy- and amino-benzoates, bactericidal aldehydes and amino acids having bactericidal properties, namely, sulfanamide, sulfathiazole, sulfaguanidine, carboxysulfathiazole, sulfadiazine, sulfamerazine, sulfapyridine and the following acids and esters: n-propyl para-hydroxy benzoate, methyl para-hydroxy benzoate, para-aminobenzoic acid, methyl para-amino benzoate, n-propyl para-amino benzoate, n-amyl para-amino benzoate, as well as urea and alloxan.

B. Anti-biotics, namely penicillins and esters thereof, streptothricin, bacitracin, streptomycin, vivicillin, gramicidin, antinomycin, tyrothricin, subtilin, tyro cidine, kojic acid, terramycin and their salts
C. Hormones, including cortisone, gonadotropic hormones, androgenic hormones, stilboestrol.

D. Pepsin, trypsin, lysozyme.

In general, the promoters may be incorporated in any of the wide variety of compositions in which cytochrome is used to eliminate infections, or stimulate the growth of normal healthy tissue, or for other therapeutic purposes.

The promoters described above when included in the cytochrome compositions as set forth activate and promote the therapeutic functions of the cytochrome.

The invention contemplates the inclusion of a number of the foregoing promoters in cytochrome compositions as well as a single individual among these promoters.

Improved properties result where a number of promoters are used because the various promoters described above exhibit different types of effects.

Referring now particularly to the sulfonamides, it is pointed out that the presence of sulfonamides having bactericidal properties in the cytochrome compositions does not adversely affect the therapeutic properties of the cytochrome. When a sulfonamide is combined with cytochrome it serves to speed the action of destroying the bacteria and thus gives the cytochrome an opportunity to make its therapeutic functions more quickly apparent. Preferred sulfonamides in accordance with the present invention include sulianilamide and sulfathiazole used either alone, or better yet, in combination.

The foregoing remarks which relate particularly to the sulfonamides are intended to be illustrative with respect to the promoters having bactericidal properties and not as an indication that the other promoters of this type do not possess similar properties since such properties are possessed by these promoters.

In contrast to the bactericidal promoters the organic sulfur compounds other than the sulphonamides such as cysteine, glutathione and allantoin function to stimulate the growth of and maintain the tone of epthellal tissue. The stimulation of the growth of epithelial tissue is much improved where one or more of these latter materials are included in the cytochrome compositions. An outstanding result of such stimulation is avoidance of the healing of wounds in such a manner as to leave unsightly scars.

The other promoters described above including hormones and the enzymes act in various ways to improve the cytochrome compositions. For example, digestive enzymes such as pepsin aid in the sloughing of dead tissue; hormones serve as nutrients for growing fibroblast and epithelial cells during healing.

For the purpose of indicating preferred methods of preparing the compositions of the present invention which have promoters incorporated therein, the following
Examples are given. It is to be understood, however, that these Examples are intended to be illustrative only and are not to be construed as limiting the scope of the invention.

EXAMPLE IX
2 grams of cytochrome were dissolved in 1000 cc. of physiological salt solution.

After the solution was thoroughly mixed it was filtered in a Buchner funnel using a double layer of filter

paper. 8 grams of sulphanilamide were then added and the solution was thoroughly agitated until the sulphanilamide was completely dissolved. The resulting solution remains sterile over long periods of time and has powerful bactericidal and therapeutic properties.

EXAMPLE X
5 grams of neutral soap powder ("Castile") and 2 grams of cytochrome were dissolved in 1000 cc. of physiological salt solution. After the solution was thoroughly mixed it was filtered through a Buchner funnel using a double layer of filter paper. 15 grams of sulfathiazole were uniformly dispersed in the solution. This composition also remains sterile over long periods of time and has powerful bactericidal and therapeutic properties.

EI;AMPLE XI
225 grams of U.S.P. white petrolatum and 900 grams of anhydrous lanolin were melted together in a double boiler. In a separate vessel a paste was formed by mixing 50 milliliters of water with a quantity of 4 grams of cytochrome. After warming the paste to the temperature of the melted material in the double boiler the paste was added thereto with vigorous stirring. 50 grams of a mixture of equal parts of finely divided sulphanilamide and sulfathiazole was mixed with 50 millilitres of water in yet another vessel. This mixture, after warming to the temperature of the melted material in the double boiler, was added to the mixture in the double boiler with vigorous stirring.

Stirring was continued until the mass had cooled to 400 C. It was then poured into tubes and jars. In addition to remaining sterile for long periods of time the resulting ointment exhibits powerful bactericidal and therapeutic properties.

EXAMPLE XII
454 grams of white beeswax were melted in a double boiler. 1630 grams of liquid petrolatum were then added. In a separate vessel 2.8 grams of sodium-borate and 6 grams of cytochrome were dissolved in 70U millilitres of water. This solution was then added to the melted mass in the double boiler with constant stirring. In yet another vessel 30 grams of a mixture of equal parts of finely divided suiphanilamide and sulfathiazole were moistened with 50 millilitres of water and the resulting mixture w

EXAMPLE XIV
A quantity of very finely divided cytochrome composition containing 1 part by weight of cytochrome, 2 parts by weight of talcum and 2 parts by weight of a finely divided mixture including equal proportions of sulphanilamide and suiphathiazole were thoroughly mixed together. The mixing was continued until a powder of relatively uniform composition was obtained. This preparation when dusted over wounds, infections and irritations not only serves to destroy any bacteria present but also stimulates the growth of normal healthy tissue.

EXAMPLE XV
20 grams of 5-carboxy sulphathiazole and 2 grams of cytochrome were dissolved in 1000 millilitres of a 5 percent solution of monosodium dihydrogen phosphate in distilled water.

EXAMPLE XVI
A composition containing 1 gram of cytochrome, 25,000 Oxford units of penicillin and 0.1 gram of vitamin E was mixed into 25 millilitres of dicthylene glycol. 0.1 gram of polyoxyalkylene derivatives of sorbitan monostearate sold under the name "Tween" (registered Trade Mark) 60 was then added. The resulting mass was added with stirring to a melted mass consisting of 25 grams of anhydrous lanolin and 50 grams of white petrolatum. Stirring was continued until the mass had cooled to 400 C.

EXAMPLE XVII
';Dermabase" 100 parts by weight
Water 2 parts by weight
Cytochrome 0.1 part by weight
Hydrocortisone Acetate 0.5 part by weight
The cytochrome is first dissolved in the water. Thereafter the "Dermabase" is melted and the aqueous solution of cytochrome and the hydrocortisone acetate added thereto. After thorough mixing and stirring the composition while molten was poured into jars and tubes where it was cooled. This preparation is particularly useful in the treatment of itchy lesions and neurodermatitis.

It has been indicated above that the promoters described herein may be added in general to any preparation including cytochrome in therapeutically effective amounts to achieve the improved results described herein. In this connection it is pointed out that if the cytochrome composition to which the

promoter is to be added does not include a solvent for the promoter in sufficient quantity to dissolve all that is added, then the promoter is dispersed in the cytochrome composition, or in the alternative, a solvent for the promoter may be added provided it is compatible with or readily dispersible in the cytochrome composition. In case the promoter exhibits a tendency to settle out or become concentrated in some part of the composition, it is preferable to add to the composition a small amount of an emulsifying agent. Such agents serve to retain the promoter in the uniformly dispersed state in which it is preferably distributed at the time of incorporation. The agents may also aid in bringing about such uniform distribution and to this end are preferably added prior to adding the promoter.

Not only may the promoters described above be added to the foregoing compositions in any desired manner and at any step of the preparation of these compositions, but in addition the proportions of the promoters to be employed in the compositions described herein may be varied considerably within the scope of the invention. To describe in detail with respect to each of the promoters included within the scope of the invention the suitable proportions and the conditions and extent under which these proportions may be varied would unduly lengthen this disclosure and serve no useful purpose. For this reason such a detailed discussion is given herein only with respect to a proportion of the promoters, it being understood that on the basis of this discussion with respect to certain promoters those skilled in the art will readily appreciate the extent to which the proportions of other promoters may be varied and the conditions under which such variations are suitable, as well as the appropriate amounts of such promoters.

Taking the sulphonamides as an example, it is pointed out that any substantial portion of a sulphonamide having bactericidal properties will exert an appreciable promoting effect upon the activity of the cytochrome composition, although the effectiveness varies somewhat depending upon the particular sulphonamide used.

Amounts of sulphanilamide as small as 0.5 percent to 1.0 percent or less by weight, based on the weight of the composition, are sufficient to have an appreciable bactericidal effect when the composition is applied to wounds. When a stronger bactericidal action is desired, amounts of sulphanilamide up to 5 percent and in severe cases up to 20 percent or higher, by weight, based on the weight of the composition, are employed. The foregoing proportions, given with respect to sulphanilamide, will indicate the appropriate proportions of various other sulphonamides to apply in any given case and more generally of various other promoters as well. The preferred proportions of the sulphonamides like the preferred proportions of the promoters generally vary with the nature of the compositions in which the promoter is included. Thus, in the more fluid compositions, particularly the aqueous compositions, the smaller proportions are generally employed, although the larger amounts may be used if desired. The less fluid compositions, such as ointments and salves, generally contain intermediate amounts but in the case of these also the amounts may be varied as desired. The larger amounts are preferably employed in the powdered compositions but in these as well as in the other types of compositions, the quantity may vary. In determining the amount of a sulfonamide to incorporate in a cytochrome composition, it should be borne in mind that the amount is generally somewhat less than would be suitable were the cytochrome not present.

It is not only possible but preferable to employ lesser amounts of the sulphonamides along with the cytochrome because sulphonamides are toxic in nature and tend to destroy tissue in contrast to the cytochrome which is non-toxic and stimulates the growth of normal healthy tissue. The primary function of the sulphonamide is to initiate the destruction of the bacteria and give the cytochrome an opportunity to exert its effect. Thus, it is not only preferable to employ the minimum quantity of sulphonamides, but it is also preferable to avoid the use of cytochrome compositions containing sulfonamides as soon as the course of the infection is definitely arrested or the danger of infection is past.

Promoters tend to make smaller amounts of cytochrome more effective and the inclusion of promoters will permit the use of smaller quantities of cytochrome without appreciable loss of effectiveness of the composition.

The cytochrome compositions including promoters are adapted for use generally as cell stimulating compositions for promoting the growth of normal, healthy cells.

They are particularly adapted for use in the treatment of infections or infectious conditions and to this end are applied locally to the affected area, such as an area of inflamed tissue, or lesion. It is preferable to employ the cytochrome compositions so as to cause the infection to heal from the base, particularly where the infection is relatively deep-seated.

Medicaments to be taken orally may have cytochrome incorporated therein as an active agent For

example, pills for treating peptic ulcer would comprise a quantity of cytochrome together with a suitable carrier and a suitable enteric covering.

It is further contemplated that the cytochrome be incorporated in suppositories for the treatment of areas best handled in this manner.

In general, the ointments and solutions discussed above are usefill to heal cuts, lesions and abrasions in any place on the body, including the feet. In treating the feet it is contemplated that various antiseptics and fungicides can be incorporated therein to deal with various infections encountered on the feet. The salves and lotions discussed above are also particularly useful when applied to burns.

WHATI CLAIM IS:

1. A cosmetical or therapeutic composition which comprises cytochrome or a cytochrome-active water-soluble derivative of cytochrome which includes the dicysteineporphyrin ring of cytochrome c distributed in a pharmaceutically acceptable carrier.

2. A composition according to claim 1, wherein the cytochrome is cytochrome c.

3. A composition according to claim 1 or 2, wherein the cytochrome has been prepared substantially according to the extraction procedure of Keilin and Hartree as hereinbefore mentioned.

4. A composition according to any of the preceding claims, wherein the carrier is viscous or powdered.

5. A composition according to any of the preceding claims, wherein the cytochrome is distributed in a pharmaceutically acceptable, viscous ointment carrier.

6. A composition according to claim 5, wherein the carrier is hydrophilic.

7. A composition according to claim 5, wherein the carrier is substantially isotonic with the body fluid of the region to which it is to be applied.

8. A composition according to claim 5, wherein the carrier is polyethylene glycol.

WARNING end of DESC field may overlap start of CLMS **.

Reivindicaciones

"WARNING" start of CLMS field may overlap end of DESC "".

effect when the composition is applied to wounds. When a stronger bactericidal action is desired, amounts of sulphanilamide up to 5 percent and in severe cases up to 20 percent or higher, by weight, based on the weight of the composition, are employed. The foregoing proportions, given with respect to sulphanilamide, will indicate the appropriate proportions of various other sulphonamides to apply in any given case and more generally of various other promoters as well. The preferred proportions of the sulphonamides like the preferred proportions of the promoters generally vary with the nature of the compositions in which the promoter is included. Thus, in the more fluid compositions, particularly the aqueous compositions, the smaller proportions are generally employed, although the larger amounts may be used if desired. The less fluid compositions, such as ointments and salves, generally contain intermediate amounts but in the case of these also the amounts may be varied as desired. The larger amounts are preferably employed in the powdered compositions but in these as well as in the other types of compositions, the quantity may vary. In determining the amount of a sulfonamide to incorporate in a cytochrome composition, it should be borne in mind that the amount is generally somewhat less than would be suitable were the cytochrome not present.

It is not only possible but preferable to employ lesser amounts of the sulphonamides along with the cytochrome because sulphonamides are toxic in nature and tend to destroy tissue in contrast to the cytochrome which is non-toxic and stimulates the growth of normal healthy tissue. The primary function of the sulphonamide is to initiate the destruction of the bacteria and give the cytochrome an opportunity to exert its effect. Thus, it is not only preferable to employ the minimum quantity of sulphonamides, but it is also preferable to avoid the use of cytochrome compositions containing sulfonamides as soon as the course of the infection is definitely arrested or the danger of infection is past.

Promoters tend to make smaller amounts of cytochrome more effective and the inclusion of promoters will permit the use of smaller quantities of cytochrome without appreciable loss of effectiveness of the composition.

The cytochrome compositions including promoters are adapted for use generally as cell stimulating compositions for promoting the growth of normal, healthy cells.

They are particularly adapted for use in the treatment of infections or infectious conditions and to this end are applied locally to the affected area, such as an area of inflamed tissue, or lesion. It is preferable to employ the cytochrome compositions so as to cause the infection to heal from the base, particularly where the infection is relatively deep-seated.

Medicaments to be taken orally may have cytochrome incorporated therein as an active agent For example, pills for treating peptic ulcer would comprise a quantity of cytochrome together with a suitable carrier and a suitable enteric covering.

It is further contemplated that the cytochrome be incorporated in suppositories for the treatment of areas best handled in this manner.

In general, the ointments and solutions discussed above are usefill to heal cuts, lesions and abrasions in any place on the body, including the feet. In treating the feet it is contemplated that various antiseptics and fungicides can be incorporated therein to deal with various infections encountered on the feet. The salves and lotions discussed above are also particularly useful when applied to burns.

WHATI CLAIM IS:

1. A cosmetical or therapeutic composition which comprises cytochrome or a cytochrome-active water-soluble derivative of cytochrome which includes the dicysteineporphyrin ring of cytochrome c distributed in a pharmaceutically acceptable carrier.

2. A composition according to claim 1, wherein the cytochrome is cytochrome c.

3. A composition according to claim 1 or 2, wherein the cytochrome has been prepared substantially according to the extraction procedure of Keilin and Hartree as hereinbefore mentioned.

4. A composition according to any of the preceding claims, wherein the carrier is viscous or powdered.

5. A composition according to any of the preceding claims, wherein the cytochrome is distributed in a pharmaceutically acceptable, viscous ointment carrier.

6. A composition according to claim 5, wherein the carrier is hydrophilic.

7. A composition according to claim 5, wherein the carrier is substantially isotonic with the body fluid of the region to which it is to be applied.

8. A composition according to claim 5, wherein the carrier is polyethylene glycol.

9. A composition according to claim 5, wherein the carrier is lanolin.

10. A cosmetical or therapeutic composition which comprises cytochrome as hereinbefore defined distributed in an emulsion of fatty acid esters and alcohols.

11. A composition according to any of the preceding claims, which contain 0.001 to 50 percent by weight of cytochrome.

12. A composition according to any of the preceding claims, which contains 0.01 to 3 percent by weight of cytochrome.

13. A composition according to claim 10, in which cytochrome c is distributed in the emulsion which is viscous and non-flowing at ordinary room temperature, in an amount of from 0.01 percent to 3 percent of the composition by weight.

14. A dentifrice comprising a pharmaceutically acceptable powder base or plastic body mass having cytochrome as hereinbefore defined distributed throughout said base or mass.

15. A dusting powder having cytochrome as hereinbefore defined distributed throughout the mass thereof.

16. A hair shampoo, hair dye or hair bleach comprising cytochrome as hereinbefore defined.

17. A hair tonic and scalp lotion comprising cytochrome as hereinbefore defined.

18. A pill for the treatment of peptic ulcer comprising cytochrome as hereinbefore defined.

19. A cosmetical or therapeutic composition which comprises cytochrome as hereinbefore defined, together with a bactericide distributed in a pharmaceutically acceptable carrier.

20. A therapeutic composition useful in treating ulcerous wounds, which comprises cytochrome as hereinbefore defined together with a promoter which enhances the therapeutic activity of the said cytochrome, said cytochrome and promoter being distributed in a viscous, pharmaceutically acceptable ointment carrier.

21, A cosmetical or therapeutic composition which comprises cytochrome as hereinbefore defined substantially as herein described with particular reference to the examples.